acknowledges, we need not reach this issue, given our conclusion that the Board did not err in finding that the Dement et al. claims were not rendered unpatentable by the FPR Publication.

VI

For the reasons set forth above, the decision of the Board is, in all respects,

AFFIRMED.

CERTIFICATE OF MAILING

I HEREBY CERTIFY THAT THIS CORRESPONDENCE IS BEING DEPOSITED WITH THE UNITED STATES POSTAL SERVICE AS FIRST-CLASS MAIL IN AN ENVELOPE ADDRESSED TO: COMMISSIONER OF PATENTS, WASHINGTON, D.C. 20231, ON 20 JUNE 1997

Mary E. McCarthy

AGENT/ATTORNEY FOR APPLICANT

20 June 1997

DATE

Attorney Docket No. P50317

IN THE UNITED STATES PATENT AND TRADEMARK OFFICE

Applicant:	Lukas-Laskey, et al.	June 20, 1997
Serial No.:	08/483,635	Group Art Unit No.: 1205
Filed:	June 7, 1995	Examiner: W. Jarvis
For:	METHOD OF TREATMENT FOR DECREASING MORTALITY RESULTING FROM CONGESTIVE HEART FAILURE	

DECLARATION OF MARTIN WEHLING

I, MARTIN WEHLING, M.D., a citizen of Germany, do hereby declare:

1. THAT I am a full professor for clinical pharmacology and director of the institute of clinical pharmacology, faculty of clinical medicine Mannheim, University of Heidelberg and that I have held this post since 1995;

2. THAT I head the division of clinical pharmacology and head the Klinische Forschergruppe (clinical research group) "clinical pharmacology", the Deutsche Forschungsgemeinschaft, and that I have held this appointment since 1994;

3. THAT I began my study of chemistry and medicine at the University of Kiel in 1975, that I received my full approbation as a physician in 1981, and that I became qualified as an internist in 1990, as a cardiologist in 1992 and as a clinical pharmacologist in 1993;

4. THAT by reason of my qualifications and experience I consider myself an expert in the field of medicine, cardiology and clinical pharmacology;

5. THAT I have read and understood the above-identified patent application and have read and understood the Office Action dated December 20, 1996;

6. THAT it has been shown in well-controlled clinical trials that neither α_1-adrenoceptor antagonists [Cohn et al., *N Engl J Med*, 314: 1547-1552 (1986)] nor a β-blocker, metoprolol, [Waagstein et al., *Lancet*, 342: 1441-1446 (1993)] decrease mortality in CHF patients; significantly

7. THAT, in my opinion based on the clinical data of known α_1-adrenoceptor antagonists and β-blockers, reduction of mortality with α-adrenoceptor antagonists or with β-blockers was an unmet need in the treatment of CHF, which could not be expected to be achieved by a combined α_1/β-blocker, such as carvedilol;

8. THAT, in my opinion based on the clinical data of known α_1-adrenoceptor antagonists and β-blockers, it would not be obvious, even to one skilled in the art, to administer an α_1/β-adrenoceptor antagonist, such as carvedilol, to decrease mortality in CHF patients;

9. THAT β-blockers have been contraindicated in patients suffering from CHF because they are known to have undesireable cardiodepressive effects;

10. THAT, in my opinion based on the data of known β-blockers, the reduction in all-cause mortality in CHF patients treated with carvedilol disclosed in the above-referenced application is unexpected and significant;

11. THAT the doses and the dosing schedules in CHF patients are quite different from those used in other indications, such as hypertension, in that the initial doses are much lower, but the target doses - after up-titration - are higher than those commonly used in hypertension;

12. THAT, in my opinion, the doses and the dosing schedules of carvedilol cannot be regarded as obvious since side-effects are avoided and reduction in mortality is achieved using doses different from those used in other indications;

13. THAT monitoring the mortality rate in the clinical trials described in the above-referenced application was not a pre-specified endpoint and that evaluating the effect of carvedilol on the survival of patients with CHF was prospectively designed into said clinical trials;

14. THAT, in my opinion, the discovery that carvedilol reduced mortality by about 67% in CHF patients satisfies a long-felt need which was recognized, but not solved, by others, as evidenced by the fact that standard agents for treating CHF, such as diuretics, digitalis glycosides, vasodilators (excluding ACE inhibitors), and ionotropic agents, relieve the symptoms of the disease, but are not known to reduce the mortality rate in CHF patients, and that even though ACE inhibitors reduce mortality in CHF patients, this reduction is only on the order of about 20%;

15. THAT certain agents, such as milrinone [Di Bianco, et al., *N Engl J Med*, 320: 677-683 (1989)], flosequinan [Anonymous, *Clin Pharmacy*, 12, 474 and 713 (1993)] and vesnarinone [Feldman, et al., *J Am Coll Cardiol*, 29, 7105 (1997)], relieve the symptoms of CHF, but increase the mortality of CHF patients;

16. THAT an independent drug safety monitoring board was installed to oversee the clinical trials described in the above-referenced application so as to stop the trials prematurely if increased mortality rates were observed in the cavedilol-treated CHF patients;

17. THAT the independent drug safety monitoring board recommended stopping the clinical trials on the basis that the placebo-treated patients, not the carvedilol-treated patients, had an excess mortality when the two groups were compared;

18. THAT, in my opinion, one of ordinary skill in the art would conclude that carvedilol exhibits a surprisingly and unexpectedly superior property when compared to other agents for treating CHF, and thus that carvedilol provides superior treatment for congestive heart failure, when compared to known agents, since it reduces mortality in CHF patients by about 67%.

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19. THAT I further declare that all the statements made herein of my knowledge are true and that all statements made on information and belief are believed to be true, and further that these statements were made with the knowledge that willful false statements and the like so made are punishable by fine or imprisonment, or both, under Section 1001 of Title 18 of the United States Code, and that such willful false statements may jeopardize the validity of the present application or of any patent issuing thereon.

Dr. Webling

Martin Webling, M.D.

6/19/97

Date

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